

## REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)

In re Application of

Application Number

07/621092

Filed

11/26/90

Group Art Unit

1812

Examiner

Wang

Paper No. 21

Assistant Commissioner for Patents  
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I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

- \_\_\_ (A) referred to in United States Patent Number \_\_\_\_\_, column \_\_\_\_\_.
- \_\_\_ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. \_\_\_\_\_, filed \_\_\_\_\_, on page \_\_\_\_\_ of paper number \_\_\_\_\_.
- \_\_\_ (C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. \_\_\_\_\_, filed \_\_\_\_\_, or
- \_\_\_ (D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

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Applicants respectfully request that the filing receipt be corrected to recite the correct filing date of November 26, 1990.

Respectfully submitted,

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**United States Patent** [19]**Barr et al.**[11] **Patent Number:** **5,460,950**[45] **Date of Patent:** **Oct. 24, 1995****[54] EXPRESSION OF PACE IN HOST CELLS AND METHODS OF USE THEREOF**

[75] **Inventors:** Philip J. Barr; Anthony J. Brake, both of Berkeley, Calif.; Randal J. Kaufman, Boston; Louise Wasley, Medfield, both of Mass.; Patricia Tekamp-Olson, San Anselmo; Polly A. Wong, Mountain View, both of Calif.

[73] **Assignees:** Genetics Institute, Inc., Cambridge, Mass.; Chiron Corporation, Emeryville, Calif.

[21] **Appl. No.:** 885,972[22] **Filed:** May 20, 1992**Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 621,092, Nov. 26, 1990, abandoned, and a continuation-in-part of Ser. No. 620,859, Nov. 29, 1990, abandoned, and a continuation-in-part of Ser. No. 621,443, Nov. 29, 1990, abandoned, and a continuation-in-part of Ser. No. 621,457, Nov. 30, 1990, abandoned.

[51] **Int. Cl.<sup>6</sup>** ..... G12N 15/00; G12N 15/57; G12N 15/81; G12N 15/85

[52] **U.S. Cl.** ..... 435/69.1; 435/69.6; 435/219; 435/226; 435/252.3; 435/320.1; 935/28; 935/32; 935/69; 935/70; 935/71; 935/60

[58] **Field of Search** ..... 435/69.1, 219, 435/226, 252.3, 320.1; 536/23.2

**[56] References Cited****U.S. PATENT DOCUMENTS**

4,652,639	3/1987	Stabinsky	536/271
4,745,051	5/1988	Smith et al.	435/69.1
4,770,999	9/1988	Kaufman et al.	435/68
4,784,950	11/1988	Hagen et al.	435/68
4,870,023	9/1989	Fraser et al.	435/320.1
4,929,553	5/1990	Bussey et al.	435/172.3
4,992,373	2/1991	Bang et al.	435/226
5,004,803	4/1991	Kaufman et al.	530/383
5,041,378	8/1991	Drummond et al.	435/234
5,059,528	10/1991	Bollen et al.	435/69.4
5,077,204	12/1991	Brake et al.	435/681

**FOREIGN PATENT DOCUMENTS**

246709	11/1987	European Pat. Off.
WO91/06314	5/1991	WIPO
US91/08725	11/1991	WIPO

**OTHER PUBLICATIONS**

Fontkamp, E., et al., 1986, DNA, 5(6):511-517.  
 Schallonen, J. A., et al., 1987, Journal of Clinical Investigation, 80:1545-1549.  
 D. C. Foster et al, Thrombosis and Haemostasis, 62:321 (1989).  
 C. K. Dexian et al, J. Biol. Chem., 264(12):6615-6618 (1989).  
 R. J. Kaufman et al, J. Biol. Chem., 261(21):9622-9628 (1986).  
 A. M. W. van den Onwelan et al, Nucl. Acids. Res., 18(3):664 (1990).  
 S. P. Smeckens et al, J. Biol. Chem., 265(6):2997-3000

(1990).

B. Furie et al, Cell, 53:505-518 (1988).

G. Thomas et al, Science, 241:226-230 (1988).

I. M. Dickerson et al, J. Biol. Chem., 265:2462 (1990).

T. Achstetter et al, EMBO J. 4:173 (1985).

K. Mizuno et al, Biochem. Biophys. Res. Commun., 144:807 (1987).

D. Julius et al, Cell, 37:1075 (1984).

D. Julius et al, Cell, 36:309 (1984).

A. J. M. Roebroek et al, EMBO J., 5:2197 (1986).

E. A. Wang et al, Proc. Natl. Acad. Sci. USA, 87:2220-2224 (1990).

R. S. Fuller et al, Proc. Natl. Acad. Sci. USA, 86:1434-1438 (1989).

I. C. Bathurst et al, Science, 235:348-350 (1987).

R. S. Fuller et al, Science, 246:482-486 (1989).

A. J. M. Roebroek et al, Molec. Biol. Rep., 11:117-125 (1986).

R. S. Fuller et al, Microbiology, 1986:273-278 (1986).

R. J. Wise et al, Proc. Natl. Acad. Sci. USA, 87:9378-9382 (1990).

R. J. Wise et al, "Expression of a Human Proprotein Processing Enzyme that Correctly Cleaves the Von Willibrand Factor Precursor at its Dibasic Amino Acid Recognition Site," The International Society of Hematology 23rd Congress the American Society of Hematology 32nd Annual Meeting (Abstract of talk at meeting 1990).

R. J. Kaufman et al, "Rate Limiting Steps in the Syntheses and Secretion of Heterologous Proteins in Mammalian Cells," The Proceedings of the Fifth European Congress of Biotechnology, Eds. Christiansen, Munck, Villadsen, Vol. 2, Munksgaard Int. Publ. Copenhagen pp. 715-719 (1990).

N. G. Seidah et al, DNA and Cell Biology, 9(6):415-424 (1990).

Y. Misumi et al, Nucleic Acid Res., 18(22):6719 (1990).

M. W. Pantoliano et al, Biochem., 26:2077-2082 (1987).

A. J. Russell et al, J. Mol. Biol., 193:803-813 (1987).

J. A. Wells et al, Proc. Natl. Acad. Sci. USA, 84:1219-1223 (1987).

Y. Ikehara et al, "Functional Expression of Furin Demonstrating its Intracellular Localization and Proprotein-Processing Activity", Abstract No. 3SC-1630, Cell Struct. Function, 16:541 (1991).

K. Hatazawa et al, "Structure and Expression of Mouse Furin, a Yeast Kex2-related Protease", J. Biol. Chem., 265(36): 22075-22078 (Dec. 25, 1990).

(List continued on next page.)

**Primary Examiner**—Robert A. Wax**Assistant Examiner**—William W. Moore**Attorney, Agent, or Firm**—Howson and Howson**[57]****ABSTRACT**

Compositions and methods are provided for endopeptidase production and for enhanced efficiencies of processing heterologous precursor polypeptides to mature polypeptides, including proteins requiring gamma-carboxylation for biological activity. These compositions and methods utilize recombinant PACE, a mammalian endopeptidase that is specific for dibasic amino acid sites.

**60 Claims, 12 Drawing Sheets**